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*Handwritten claim changes*

(1)

Amendment C

Paper No. 14

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

Jan Vijg

Serial No.: 09/306,333

Filed: May 6, 1999

Group Art Unit: 1855

Examiner: Souaya, J.

For: BRCA1 and hMLH1 Gene Primer Sequences And Method For Testing

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Hon. Commissioner of Patents  
and Trademarks  
Washington, DC 20231

Sir:

Replying to the Office communication of July 31, 2001, please amend the  
application as follows:

Please delete SEQID NOS 121 and 122 in the clamping sequence listings as  
erroneously inadvertently listed.

Please amend claim 10 as follows:

-10. (Amended) A method for detecting mutations in BRA1 genes comprising providing  
PCR primers capable of amplifying the entire coding sequence of the BRCA1 genes;

amplifying a test sample containing nucleotide sequences by long distance multiplex PCR  
with primers *exon fragments using primer sequences SEQID Nos. 37-46* as listed in Table 2, producing a first set of amplification products; *✓*

this first set of amplification products to short distance multiplex PCR to produce a second  
set of amplification products *with exon fragments using primer sequences SEQID No. 47-120* using the primer pairs of Table 4 listed under the "PRIMER  
SEQUENCES" column with clamping and linking sequences listed under the "CLAMPING  
SEQUENCES" column *that further include two clamping sequences* *✓*

for each a plurality of the exon fragments, including clamping sequences *SEQID Nos. 27 and 30,*  
*29 and 31, 27 and 32 and 29 and 31, such*

~~SEQUENCE column of Table 4~~ for effecting this short distance PCR; and subjecting

the second set of amplification products to two-dimensional gel electrophoresis to produce a characteristic spot pattern for a specific mutation in the BRCA1 gene.—

Please amend claim 4 as follows:

—4. (Amended) Test kits for enabling BRCA1 gene testing comprising primer ~~polymers~~<sup>S SEQ ID No. 47</sup> in  
~~Table 4 under PRIMER SEQUENCE column~~, mixed in about 20mM of Tris-HCl, 50mM  
KCl, 25 $\mu$ M of dNTP and 5% formamide.—

OCT 26 2001 14:51 FR RINES AND RINES

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Certification

USSN 09/306,333 October 26, 2001--Vijg et al

I hereby certify that the attached amendment document is being  
facsimile transmitted to the USPTO under date of October 26, 2001.

*Holly Foote*

Holly Foote  
RINES & RINES  
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Concord, NH 03301

Amendment D

Paper No. 16

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

Jan Vijg

Serial No.: 09/306,333

Filed: May 6, 1999

Group Art Unit: 1655

Examiner: Souaya, J.

For: BRCA1 and hMLH1 Gene Primer Sequences And Method For Testing

\*\*\*

Hon. Commissioner of Patents  
and Trademarks  
Washington, DC 20231

Please amend claim 10 as follows:

Sub  
G1

E1

-10. A method of detecting mutations in BRA1 genes comprising providing PCR primers capable of amplifying the entire coding sequence of the BRCA1 genes; amplifying a test sample containing nucleotide sequences by long distance multiplex PCR with exon fragments using primer sequences SEQ. ID Nos. 37-46, producing a first set of amplification products; subjecting this first set of amplification products to short distance multiplex PCR to produce a second set of amplification products with exon fragments using primer sequences SEQ ID Nos. 47-120 and with clamping and linking sequences therefor that include two clamping sequences for each of a plurality of the exon fragments, including clamping sequences SEQ ID Nos. 27 and 30, 29 and 31, 27 and 32, and 27 and 31, such effecting said short distance PCR; and subjecting the second set of amplification products to two-dimensional gel electrophoresis to produce a characteristic spot pattern for a specific mutation in the BRCA1 gene.

Please amend claim 4 as follows:

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4. Test kits for enabling BRCA1 gene testing comprising primers SEQ. ID Nos. 47-120 mixed in about 20mM of Tris-HCl, 50mM KCl, 25pM of dNTP and 5% formamide. --

✓ Claim 11, line 2, cancel "and hMLH1".

REMARKS

It is desired to thank the Examiner for helpful suggestions for rendering the claims more definite and more definitive of applicant's provision of two clamps on primer exons that led to the unobvious result of vastly improved resolution of the electrophoresis patterns, as set forth in the earlier submitted Declaration.

Reconsideration and allowance accordingly now appear to be in order and are therefore respectfully requested.

Any costs incurred by this filing, including for any required extension(s) of time, petition for which is hereby made, may be charged to account No. 18-1425 of the undersigned attorneys.

Respectfully submitted,

RINES AND RINES

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Registration No. 15,932

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